I spy with my little eye something beginning with S

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I spy with my little eye something beginning with S: Spotting sepsis

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Editorial

The first step in the management of a condition is spotting it, but in the case of sepsis this can prove difficult. Earlier this year the International Consensus definitions of sepsis changed, with emphasis moving away from the inflammatory response towards organ dysfunction resulting from infection, and the term severe sepsis being made redundant[1]. The criteria for systemic inflammatory response are present in as many as four out of five critically ill patients and lacks diagnostic accuracy[2]. The new definition now focuses on the presence of organ dysfunction and whether it may have resulted from infection. There has already been significant debate about the validity of this new definition, largely evidenced by data from in-hospital care in parts of North America[3,4]. However, the major emphasis of the new definition is on a simplified system for early suspicion of organ dysfunction resulting from suspected infection, rather than a precise pathological definition for sepsis. Despite high predictive value (AUROC = 0.81; 95% CI, 0.80-0.82)[5], critics of the new definition have highlighted that the use of qSOFA score has not been fully validated in the various clinical settings where sepsis may present[4] It has also been pointed out that low income countries were not involved in the new consensus process where early diagnosis and awareness are key to sepsis management[4]. The change in definitions could mean that findings from previous large international research studies may need to be re-interpreted. Considering that such debate remains about the definitions of sepsis and their purpose, how can clinicians, or indeed the public, be expected to spot it with confidence?

Recognising sepsis as a clinician

The Surviving Sepsis Campaign has helped to put sepsis at the forefront of clinician's minds, but mortality and morbidity from sepsis remains excessively high. Hospital mortality from sepsis is quoted as 25-30% and higher at 40-50% if patients have septic shock[6,7]and patients who survive an episode of sepsis have a significant excess risk of mortality for a prolonged period of time[8,9]. High quality care must begin with accurate diagnosis, yet there are still accounts of cases of unrecognised sepsis, as highlighted by the recent reports by the Parliamentary and Health Service Ombudsman and the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) [10,11]. These reports demonstrate that there are shortcomings in both the public's and healthcare professionals' knowledge of sepsis, adding to the likelihood of cases of sepsis presenting late or its diagnosis being missed altogether[12] . Furthermore, competing demands on time and resources, busy staff and an overburdened healthcare system can all contribute to late recognition and delayed management of sepsis.

What may still prove difficult is catching those patients in the very early stages of sepsis. Despite on-going research, a diagnostic clinical or biochemical biomarker for sepsis continues to elude us[13].Ideally, a test of some sort is needed to say definitively "this patient has sepsis" or to exclude it, but due to the heterogeneity of sepsis as a syndrome, there are no tests with the necessary sensitivity and specificity in existence[14]. The lack of precise diagnostic criteria or definition also impacts on clinical research development, in particular making the identification of cases, evaluation of the efficacy of treatment and assessment of patient outcomes more problematic. Without the appropriate and timely diagnosis of sepsis, clinical trials investigating novel biomarkers remain methodologically challenging.

How can we improve our ability to spot sepsis? New draft guidelines from the National Institute for Health and Care Excellence (NICE) include recommendations on when to suspect sepsis, highlighting the need to be vigilant when symptoms are vague[15]. Whilst this may help to raise the suspicion of sepsis earlier, it still relies on clinicians' ability to spot the diagnosis. One approach to overcome this issue involves the utilisation of electronic recording of observations, where an alert is activated when the patient's observations suggest sepsis[16]. This may at least flag these patients to healthcare

professionals, so that appropriate investigations and further management can be implemented in a timely fashion. This does away with some of the human error involved in monitoring patients, but correct management will still require engagement and appropriate actions from clinicians on the findings.

"Can I catch it?" – Public understanding of sepsis

In a recent study of survivors of severe sepsis there were a number of patients that had not even known that they had been treated for sepsis until they were approached by the study investigators[17]. Considering the lack of understanding of those with first-hand experience of the condition, it is unsurprising to think that the general public is disadvantaged when it comes to awareness of sepsis. Questions from members of the public at a recent patient and public involvement meeting that one author attended included "can I catch it?", demonstrating the conceptual difficulties and challenges for healthcare professionals in communicating messages about sepsis.

There has recently been media attention to sepsis due to some high profile cases, such as William Mead and Charlie Jermyn, both of whom were children. This helps to raise the public profile of sepsis, but will not improve the public's ability to recognise the syndrome. It also demonstrates the additional difficulty of diagnosing sepsis in children; NICE guidelines highlight the very young as an at risk population for the development of sepsis, with the extra complexity of different signs and symptoms of sepsis compared to adults[15]. Yet the new definitions of sepsis focus on adult patients only; the diagnostic criteria has not been validated in children, and would be inappropriate considering the differing physiological parameters found in children of different ages[1]. However, the new NICE guidelines on sepsis do focus on clinical signs and symptoms in children that are suspicious of sepsis, and includes guidance on the management of sepsis in children[15]. An international definition for sepsis in children is needed to ensure prompt recognition and management of sepsis in children worldwide.

Public campaigns to improve recognition of other diseases such as myocardial infarction and stroke have helped to improve mortality in these areas through earlier treatment due to prompt recognition[18]. NHS England has stated that it will support the development of a public awareness campaign on sepsis amongst vulnerable groups and the UK Sepsis Trust has developed a list of warning signs to look out for with the acronym S.E.P.S.I.S., in the same vein as the F.A.S.T. signs for stroke[11]. However, the early symptoms of sepsis are vague, often resembling less severe illnesses such as a common cold, making it difficult for lay people and healthcare professionals alike to discriminate a bout of 'man-flu' from life-threatening sepsis. More research is required to explore the public understanding of sepsis and it's definition to help guide a systematic public awareness programme.

The future for spotting sepsis

Only time can tell what impact the new definition will have on the recognition of sepsis, although the current revision has been focused on delivering improved awareness of the syndrome, providing potentially improved functionality for healthcare professionals. Research aimed at investigating the diagnostic utility of the new definitions in other jurisdictions and care settings outside of hospital are urgently required.

Increasing clinician recognition of sepsis requires further training and education, as well as research into potential biomarkers of relevance to the recognition and treatment of sepsis. In particular, emerging rapid biomarkers of infection could contribute significantly to diagnosis and theranosis for sepsis, but according to NICE require better evidence of clinical and cost effectiveness before routine service adoption[15, 19,20].

Public understanding of sepsis can only realistically be improved through national media campaigns, but it's still unclear what the message should be – if a healthcare professional can't spot it, how can a lay person be expected to recognise sepsis? Further research should look for potential gaps in public understanding, allowing any future media campaigns to be tailored to those knowledge gaps.

Most of the data on sepsis is from the Critical Care setting[21], yet it is on the wards and pre-hospital where sepsis develops but is not recognised. Further data is needed on sepsis in the non-Critical Care setting so that the full extent of the prevalence of sepsis can be appreciated. Until we can definitively recognise and diagnose sepsis both pre-hospital and in the hospital, we will continue to miss cases, leading to increased morbidity and mortality from the disease. In the meantime, we must focus our attention on continuing to raise awareness of sepsis, putting sepsis at the forefront of our minds and in our lists of differentials, so that the highest quality care can be delivered, resulting in the best patient outcomes.

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1 Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;**315**:801–10

2 Kaukonnen KM, Bailey M, Pilcher D, Cooper J, Bellomo R. Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis. *N Engl J Med* 2015; **372**:1629-1638.

3 Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;**315**:762–74

4 Abraham E. New Definitions for Sepsis and Septic Shock: Continuing Evolution but With Much Still to Be Done. *JAMA* 2016;**315**:757–9

5 Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA 2016*;**315**:762-74

6 Kaukonen KM, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA* 2014; **311**:1308-16

7Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, Reinhart K, Antonelli M, Pickkers P, Njimi H, Jimenez E, Sakr Y; Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med* 2014;**2**:380-6

8 Prescott HC, Osterholzer JJ, Langa KM, Angus DC, Iwashyna TJ. Late mortality after sepsis: propensity matched cohort study. *Br Med J* 2016;**353**:i2375

9 Brett SJ. Late Mortality after Sepsis. *Br Med J* 2016;**353**:i2735

10 Parliamentary and Health Service Ombudsman. Time to Act Severe Sepsis: rapid diagnosis and treatment saves lives. September 2013

11 National Confidential Enquiry into Patient Outcome and Death. Just Say Sepsis! A review of the process of care received by patient with sepsis. 2015

12 Jeffery AD, Mutsch KS, Knapp L. Knowledge and Recognition of SIRS And Sepsis among Pediatric Nurses. *Pediatr Nurs*; 2014;**40**:271-8

13 Pierrakos C, Vincent JL. Sepsis biomarkers: a review. *Crit Care* 2010;**14**:R15

14 Cohen J, Vincent JL, Adhikari NKJ, Machado FR, Angus DC, Calandra T, Jaton K, Giulieri S, Delaloye J, Opal S, Tracey K, van der Poll T, Pelfrene E. Sepsis: a roadmap for future research. *Lancet Infect Dis* 2015;**15**: 581–614

15 NICE. Sepsis: recognition, diagnosis and early management. NICE guideline [NG51]. Available from https://www.nice.org.uk/guideline/ng51/resources/sepsis-recognition-diagnosis-and-early-management-1837508256709 (accessed 16 July 2016)

16 Amland RC, Lyons JJ, Greene TL, Haley JM. A two-stage clinical decision support system for early

recognition and stratification of patients with sepsis: an observational cohort study. *J R Soc Med Open* 2015; **6**: 1–10
17 Gallop KH, Kerr CE, Nixon A, Verdian L, Barney JB, Beale RJ. A qualitative investigation of patients' and caregivers' experiences of severe sepsis. *Crit Care Med* 2015; **43**:296-307
18 Rubulotta FM, Ramsay G, Parker MM, Dellinger RP, Levy MM, Poeze M. An international survey: Public awareness and perception of sepsis. *Crit Care Med* 2009;**37**:167-70.
19 NICE. Tests for rapidly identifying bloodstream bacteria and fungi (LightCycler SeptiFast Test MGRADE, SepsiTest and IRIDICA BAC BSI assay) NICE diagnostics guidance [DG20]. Available from https://www.nice.org.uk/guidance/dg20 (accessed 11 May 2016)
20 NICE. Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) NICE diagnostics guidance [DG18]. Available from https://www.nice.org.uk/guidance/dg18 (accessed 11 May 2016)
21Rhodes A, Phillips G, Beale R, Cecconi M, Chiche JD, De Backer D, et al. The Surviving Sepsis Campaign bundles and outcome: results from the International Multicentre Prevalence Study on Sepsis (the IMPreSS study). *Intensive Care Med* 2015;**41**:1620–8